REMARKS

Applicants have canceled claims 11-25, 27 and 32-35, drawn to non-elected subject matter, without prejudice. Applicants reserve their right to pursue the non-elected subject matter in any application(s) claiming benefit herefrom under 35 U.S.C. § 120.

Applicants have amended claim 10 to recite the term "polypeptide" to modify "TRELL".

Applicants have amended claim 28 to add the terms "the steps of" to the recited method of expressing a TRELL polypeptide.

None of these amendments constitutes new matter.

Claims 1-4, 6-8, 10, 28, 30, 31 and 39-47 are pending in this application. All of these claims stand rejected as being unpatentable under 35 U.S.C. § 112, first paragraph. As discussed more fully below, applicants traverse this rejection.

THE OFFICE ACTION

The Drawings

The Office Action refers to the drawings filed on February 5, 1999 but does not indicate the status of their acceptance. Applicants request that the Examiner indicate that status in the next Official Communication in this application.

The Priority Claim

Applicants note the Examiner's acknowledgement of the claim for domestic priority under U.S.C. § 119(e). The instant application also claims priority under 35 U.S.C. § 120 from PCT patent application PCT/US97/13945, filed August 7, 1997. See the Declaration/Power of Attorney of record herein, as well as the "Related Applications" paragraph added to page 1 of the specification in an Amendment and Request for Reconsideration dated October 11, 2001. Applicants request that the Examiner acknowledge the 35 U.S.C. § 120 priority claim in the next Official Communication in this application.

THE REJECTIONS

ENABLEMENT

Claims 1-4, 6-8, 10, 28, 30, 31 and 39-47 stand rejected under 35 U.S.C. § 112, first paragraph, for purportedly lacking enablement. More particularly, the Examiner contends that "one of skill in the art could not use the claimed invention without performing undue experimentation". Applicants disagree.

The starting point for assessing enablement, or lack thereof, is the "claimed invention". 35 U.S.C. § 112, first paragraph. At the outset, applicants point out that the pending claims are directed to nucleic acids encoding TRELL polypeptides, as well as vectors comprising those nucleic acids, hosts transformed with those vectors and methods using them to produce the TRELL polypeptides. The Examiner has cited no scientific evidence establishing that a person of skill in the art, at applicants' effective filing date, would need to resort to undue experimentation to make or use the nucleic acids, vectors, hosts or methods of the pending claims. Nor has the Examiner cited any evidence that the instant specification omits "any specific

starting material or any of the conditions under which a process can be carried out." Genentech, Inc. v. Novo Nordisk A/S, 108 F.3d 1361, 1366, 42 USPQ2d 1001, 1005 (Fed. Cir. 1997). In the absence of such evidence, the § 112 rejection is without basis, as a matter of science and law.

Discounting such evidence, the Examiner's contention of non-enablement turns on three assertions: (1) the *in vivo* biological function of TRELL was unknown at the time of the invention; (2) no clear association was established between TRELL and any disease or disorder and (3) applicants' demonstration that TRELL kills HT29-14 cells serves only to learn more about how TRELL functions. As discussed herein and in the Declaration of Jeffrey Browning, Ph.D., ("Browning Declaration"), filed concurrently herewith, the Examiner's assertions are without merit.

The Browning Declaration demonstrates that a person of skill in the art, following the teachings of the specification, would appreciate the biological function of TRELL and the types of diseases and conditions associated therewith. Based on that appreciation, a person of skill in

the art would be able to use applicants' nucleic acids encoding TRELL polypeptides, as well as the TRELL polypeptides themselves, to develop therapeutics, diagnostics or drug targets.

As demonstrated in the Browning Declaration, based on the teachings in the application, a person of skill in the art would appreciate a potential role of TRELL in the immune system and diseases associated therewith (Browning Declaration, ¶¶ 8-11). Specifically, the Browning Declaration details studies disclosed in the application, as well as additional confirmatory studies, evidencing the biological activity of TRELL polypeptides and hence, the utility of nucleic acids which encode the TRELL polypeptides, by the ability of TRELL polypeptides to induce cytotoxic activity in tumor cell lines (Browning Declaration, ¶¶ 10-15). Furthermore, as discussed in the Browning Declaration, additional confirmatory studies have demonstrated an *in vivo* biological function for TRELL polypeptides and hence, the utility of nucleic acids which encode the TRELL polypeptides (Browning Declaration, ¶¶ 17-19). Specifically, further confirmation of a role of TRELL

in the development of a number of other immune-associated diseases is demonstrated by the ability of anti-TRELL antibodies to detect aberrant TRELL polypeptide levels in immune-associated diseases, such as lupus, and the ability of those antibodies to alleviate disease severity in conventional *in vivo* immune-related disease models, such as those for arthritis and stroke (Browning Declaration, ¶¶ 17-19).

The Examiner asserts that the application establishes no clear association between TRELL and any disease or disorder. Applicants disagree. As discussed above, the Browning Declaration demonstrates that a person of skill in the art, following the teachings of the application, would appreciate that TRELL is associated with the development of immune-associated diseases (Browning Declaration, ¶¶ 8-19). Specifically, the Browning Declaration describes an association between TRELL and the development and progression of a number of immune-associated diseases, such as cancer, lupus, arthritis and stroke (Browning Declaration, ¶¶ 8-11 and 15-19).

The Examiner also contends that applicants' demonstration that TRELL kills HT29-14 cells serves only to learn more about how TRELL functions. Specifically, the Examiner discounts the cytotoxicity assay in the HT29-14 cell line on the basis that the structure of the TRELL polypeptide was not disclosed and the relevance of HT29-14 cells to disease is unclear because *in vitro* cell lines are a poor representation of malignancy, with characteristics profoundly different from the human disease (citing Dermer, Biotechnology (1994) 12: 320). Applicants disagree.

First, with reference to the specification, the Browning Declaration makes clear which TRELL polypeptide was used in the HT29-14 cell assays (Browning Declaration, ¶ 12). Secondly, the Browning Declaration demonstrates that a person of skill in the art would appreciate the utility of the HT29-14 cell line for assessing a potential anti-tumor agent and confirms its use in the art to evaluate the efficacy of potential anti-cancer drugs (Browning Declaration, ¶¶ 13-16). Moreover, the Browning Declaration discusses additional *in vitro* data in other tumor cell lines that a person of skill in the art would appreciate to be of

use for assessing potential anti-tumor agents, such as TRELL (Browning Declaration, ¶ 15). The Browning Declaration further describes the ability of TRELL polypeptides to induce cytotoxicity in these tumor cell lines in the presence or absence of IFN-γ (Browning Declaration, ¶ 15).

Finally, the Browning Declaration (¶ 18) provides evidence regarding the utility of TRELL in diagnostics for immune-associated diseases.

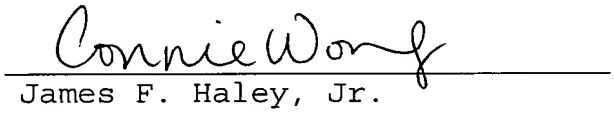
For all the foregoing reasons, a person of ordinary skill in the art, following the teachings of the application would appreciate the biological function of TRELL and the types of diseases associated with TRELL. Specifically, applicants have disclosed and demonstrated the role of TRELL in the development of a number of immune-associated diseases, as illustrated by the cytotoxic activity induced in *in vitro* tumor cell lines, as well as the ability of blocking antibodies to alleviate the severity of diseases, such as arthritis and stroke *in vivo*. Claims 1-4, 6-8, 10, 28, 30, 31 and 39-47 are sufficiently enabled.

Accordingly, the rejection based on 35 U.S.C. § 112, first paragraph, should be withdrawn.

CONCLUSIONS

For the foregoing reasons, applicants believe the claims to be in condition for allowance and request that this application be passed to issue.

Respectfully submitted,



James F. Haley, Jr.
(Reg. No. 27,794)
Margaret A. Pierri
(Reg. No. 30,709)
Attorneys for Applicants
Connie Wong
(Limited Recognition)
Agent for Applicants
FISH & NEAVE
Customer No. 1473
1251 Avenue of the Americas
New York, New York 10020-1105
Tel.: (212) 596-9000
Fax: (212) 596-9090